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## SEQUENCE LISTINGS

<110> ELI LILLY AND COMPANY

<120> RECOMBINANT PROTEIN POSSESSING HUMAN HEPATITIS C VIRUS RNA-DEPENDENT POLYMERASE ACTIVITY AND METHOD OF PRODUCING THE SAME

<130> 660950

<150> JP 10/047015

<151> 1998-2-27

<160> 19

<210> 1

<211> 1733

<212> DNA

<213> Hepatitis C virus JK-1 (NS5B)

<400> 1

tcg atg tct tac acg tgg aca ggc gcc cta atc aca cca tgc gcc gcg 48

Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala

1 5 10 15

gag gag agc aag ctg ccc atc aat ccg ttg agc aac tct ttg ctg cgt 96

Glu Glu Ser Lys Leu Pro Ile Asn Pro Leu Ser Asn Ser Leu Leu Arg

20 25 30

cac cac aac atg gtc tac gcc aca aca tct cgc agc gca ggc cta cgg 144

His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg

35 40 45

cag aaa aag gtc acc ttt gac aga ctg cag gtc ccg gac gac cat tac 192

Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Pro Asp Asp His Tyr

50 55 60

cgg gac gtg ctc aag gag atg aag gcg aag gcg tcc aca gtt aag gct 240

Sequence 1266950

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|--|-----|
| Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala                |     |
| 65                      70                      75                      80     |     |
| aaa ctt cta tct gta gaa gaa gcc tgc aag ctg acg ccc cca cac tcg                | 288 |
| Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His Ser                |     |
| 85                      90                      95                             |     |
| gcc aga tcc aaa ttt ggc tat ggg gcg aag gac gtc cgg aac cta tcc                | 336 |
| Ala Arg Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser                |     |
| 100                      105                      110                          |     |
| agc aag gcc gtt aac cac atc cac tcc gtg tgg aag gac ttg ctg gaa                | 384 |
| Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu                |     |
| 115                      120                      125                          |     |
| gac act gaa aca cca att gac act acc atc atg gca aaa aat gag gtc                | 432 |
| Asp Thr Glu Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val                |     |
| 130                      135                      140                          |     |
| ttc tgt gtt caa cca gag aaa gga ggc cgc aag cca gcc cgc ctt atc                | 480 |
| Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile                |     |
| 145                      150                      155                      160 |     |
| gta ttc cca gaa ctt ggg gtt cgt gtg tgc gag aaa atg gcc ctt tac                | 528 |
| Val Phe Pro Glu Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr                |     |
| 165                      170                      175                          |     |
| gac gtg gtc tcc act ctt cct cag gcc gtg atg ggc tcc tca tac gga                | 576 |
| Asp Val Val Ser Thr Leu Pro Gln Ala Val Met Gly Ser Ser Tyr Gly                |     |
| 180                      185                      190                          |     |
| ttc cag tac tct cct ggg cag cgg gtc gag ttc ctg gtg aat gcc tgg                | 624 |
| Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Ala Trp                |     |
| 195                      200                      205                          |     |
| aaa tcg aag aaa aac cct atg ggc ttc gca tat tgc acc cgc tgt ttt                | 672 |

|   |      |
|---|------|
| Lys Ser Lys Lys Asn Pro Met Gly Phe Ala Tyr Cys Thr Arg Cys Phe |      |
| 210   | 215  |
| 220   |      |
| gac tca acg gtc act gag agt gat atc cgt gtt gag gag tca att tac | 720  |
| Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Val Glu Glu Ser Ile Tyr |      |
| 225   | 230  |
| 235   | 240  |
| caa tgt tgt gac ttg gcc ccc gag gcc aga cag gtc ata agg tcg ctc | 768  |
| Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Val Ile Arg Ser Leu |      |
| 245   | 250  |
| 255   |      |
| acg gag cgg ctt tat atc ggg ggc ccc ctg act aat tca aaa ggg cag | 816  |
| Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln |      |
| 260   | 265  |
| 270   |      |
| aac tgc ggt tat cgc cgg tgc cgc gcc agc ggt gtg ctg acg act aac | 864  |
| Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Asn |      |
| 275   | 280  |
| 285   |      |
| tgc ggt aat acc ctc aca tgt tac ttg aag gcc tct gca gcc tgt cga | 912  |
| Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg |      |
| 290   | 295  |
| 300   |      |
| gct gca aag ctc cag gac tgc acg atg ctc gtg tgc gga gac gac ctt | 960  |
| Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu |      |
| 305   | 310  |
| 315   | 320  |
| gtc gtt atc tgt gaa agc gcg gga acc cag gag gac gcg gcg agc cta | 1008 |
| Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu |      |
| 325   | 330  |
| 335   |      |
| cga gtc ttc acg gag gct atg act agg tac tct gcc ccc ccc ggg gac | 1056 |
| Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp |      |
| 340   | 335  |
| 350   |      |
| ccg ccc caa cca gaa tac gac ttg gag tta ata aca tca tgc tcc tcc | 1104 |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|--|
| Pro | Pro | Gln | Pro | Glu | Tyr | Asp | Leu | Glu | Leu | Ile | Thr | Ser | Cys | Ser | Ser |      |  |
| 355 |     |     |     | 360 |     |     |     | 365 |     |     |     |     |     |     |     |      |  |
| aac | gtg | tcg | gtc | gcg | cac | gac | gca | tct | ggc | aag | cgg | gtg | tac | tac | ctc | 1152 |  |
| Asn | Val | Ser | Val | Ala | His | Asp | Ala | Ser | Gly | Lys | Arg | Val | Tyr | Tyr | Leu |      |  |
| 370 |     |     |     | 375 |     |     |     | 380 |     |     |     |     |     |     |     |      |  |
| act | cgc | gac | ccc | acc | acc | ccc | ctc | gcg | agg | gca | gcg | tgg | gaa | aca | gca | 1200 |  |
| Thr | Arg | Asp | Pro | Thr | Thr | Pro | Leu | Ala | Arg | Ala | Ala | Trp | Glu | Thr | Ala |      |  |
| 385 |     |     |     | 390 |     |     |     | 395 |     |     |     | 400 |     |     |     |      |  |
| aga | cac | act | cca | gta | aac | tcc | tgg | cta | ggc | aac | atc | atc | atg | tac | gcg | 1248 |  |
| Arg | His | Thr | Pro | Val | Asn | Ser | Trp | Leu | Gly | Asn | Ile | Ile | Met | Tyr | Ala |      |  |
| 405 |     |     |     | 410 |     |     |     | 415 |     |     |     |     |     |     |     |      |  |
| ccc | acc | ctg | tgg | gca | agg | atg | att | ctg | atg | acc | cac | ttc | ttc | tcc | atc | 1296 |  |
| Pro | Thr | Leu | Trp | Ala | Arg | Met | Ile | Leu | Met | Thr | His | Phe | Phe | Ser | Ile |      |  |
| 420 |     |     |     | 425 |     |     |     | 430 |     |     |     |     |     |     |     |      |  |
| ctt | cta | gct | cag | gag | caa | ctt | gaa | aaa | gcc | ctg | ggg | tgt | cag | atc | tac | 1344 |  |
| Leu | Leu | Ala | Gln | Glu | Gln | Leu | Glu | Lys | Ala | Leu | Gly | Cys | Gln | Ile | Tyr |      |  |
| 435 |     |     |     | 440 |     |     |     | 445 |     |     |     |     |     |     |     |      |  |
| ggg | gcc | act | tac | ttc | att | gaa | cca | ctt | gac | cta | cct | cag | atc | att | cag | 1392 |  |
| Gly | Ala | Thr | Tyr | Phe | Ile | Glu | Pro | Leu | Asp | Leu | Pro | Gln | Ile | Ile | Gln |      |  |
| 450 |     |     |     | 455 |     |     |     | 460 |     |     |     |     |     |     |     |      |  |
| cga | ctc | cac | ggg | ctt | agc | gca | ttt | tca | ctc | cac | agt | tac | tct | cca | ggg | 1440 |  |
| Arg | Leu | His | Gly | Leu | Ser | Ala | Phe | Ser | Leu | His | Ser | Tyr | Ser | Pro | Gly |      |  |
| 465 |     |     |     | 470 |     |     |     | 475 |     |     |     | 480 |     |     |     |      |  |
| gaa | atc | aat | agg | gtg | gct | tca | tgc | ctc | agg | aaa | ctt | ggg | gta | cca | ccc | 1488 |  |
| Glu | Ile | Asn | Arg | Val | Ala | Ser | Cys | Leu | Arg | Lys | Leu | Gly | Val | Pro | Pro |      |  |
| 485 |     |     |     | 490 |     |     |     | 495 |     |     |     |     |     |     |     |      |  |
| ttg | cga | gtc | tgg | aga | cat | cgg | gcc | aga | agt | gtc | cgc | gct | aag | cta | ctg | 1536 |  |

<210> 2

<211> 591

<212> PRT

<213> Hepatitis C virus JK-1 (NS5B)

<400> 2

Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala  
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Glu Glu Ser Lys Leu Pro Ile Asn Pro Leu Ser Asn Ser Leu Leu Arg  
20 25 30

His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg

|   |     |     |
|---|-----|-----|
| 35  | 40  | 45  |
| Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Pro Asp Asp His Tyr |     |     |
| 50  | 55  | 60  |
| Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala |     |     |
| 65  | 70  | 75  |
| Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His Ser |     |     |
| 85  | 90  | 95  |
| Ala Arg Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser |     |     |
| 100   | 105 | 110 |
| Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu |     |     |
| 115   | 120 | 125 |
| Asp Thr Glu Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val |     |     |
| 130   | 135 | 140 |
| Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile |     |     |
| 145   | 150 | 155 |
| Val Phe Pro Glu Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr |     |     |
| 165   | 170 | 175 |
| Asp Val Val Ser Thr Leu Pro Gln Ala Val Met Gly Ser Ser Tyr Gly |     |     |
| 180   | 185 | 190 |
| Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Ala Trp |     |     |
| 195   | 200 | 205 |
| Lys Ser Lys Lys Asn Pro Met Gly Phe Ala Tyr Cys Thr Arg Cys Phe |     |     |
| 210   | 215 | 220 |
| Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Val Glu Glu Ser Ile Tyr |     |     |
| 225   | 230 | 235 |
| Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Val Ile Arg Ser Leu |     |     |
| 245   | 250 | 255 |

Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln  
 260 265 270  
 Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Asn  
 275 280 285  
 Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg  
 290 295 300  
 Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu  
 305 310 315 320  
 Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu  
 325 330 335  
 Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp  
 340 335 350  
 Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser  
 355 360 365  
 Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu  
 370 375 380  
 Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala  
 385 390 395 400  
 Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala  
 405 410 415  
 Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile  
 420 425 430  
 Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Gly Cys Gln Ile Tyr  
 435 440 445  
 Gly Ala Thr Tyr Phe Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Gln  
 450 455 460  
 Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly

300  
 310  
 320  
 330  
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 440  
 450  
 460



465                      470                      475                      480  
 Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro  
                          485                      490                      495  
 Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Lys Leu Leu  
                          500                      505                      510  
 Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp  
                          515                      520                      525  
 Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser Gln  
                          530                      535                      540  
 Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile  
 545                      550                      555                      560  
 Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Trp Cys Leu  
                          565                      570                      575  
 Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg  
                          580                      585                      590

&lt;210&gt; 3

&lt;211&gt; 111

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;400&gt; 3

tcg gat ctg gtt ccg cgt gga tcg tgc acg aat tta cgt cgt gca tct      48  
 Ser Asp Leu Val Pro Arg Gly Ser Cys Thr Asn Leu Arg Arg Ala Ser  
     1                      5                      10                      15  
 gtt ctg aat tcg agc tcc ggt acc ccc ggg gtc gac gga tcc caa ttc      96  
 Val Leu Asn Ser Ser Ser Gly Thr Pro Gly Val Asp Gly Ser Gln Phe  
                          20                      25                      30  
 atc gtg act gac tga      111

35

**<211> 37**

## <212> DNA

### <213> Artificial Sequence

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gaattcgagc tccggtaccc ccggggtcga cggatcc

37

<210> 5

&lt;211&gt; 37

<212> DNA

### <213> Artificial Sequence

<400> 5

ggatccgtcg accccggggg taccggagct cgaattc

37.

**<210> 6**

&lt;211&gt; 33

## <212> DNA

### <213> Artificial Sequence

**<400> 6**

gggagctcca tgtcgatgtc ttacacgtgg aca

33

**<210> 7**

&lt;211&gt; 32

## <212> DNA

### <213> Artificial Sequence

<400> 7

gggtcgacc c ggttggggag caggtagatg cc

32

<210> 8

<211> 32

<212> DNA

<213> Artificial Sequence

<400> 8

gggtcgacgc ggggtcgggc acgagacagg ct

32

<210> 9

<211> 27

<212> DNA

<213> Artificial Sequence

<400> 9

gcggatccag atctacgggg ccactta

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<210> 10

<211> 29

<212> DNA

<213> Artificial Sequence

<400> 10

gcgaattcaa gacaaaggga atggcctat

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<211> 82

<212> DNA

<213> Artificial Sequence

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60

tttttcttt ttttttttt ct

82

<210> 12

<211> 80

<212> DNA

<400> 12

aaaaaaaaagg aaaaaaaaga 80

&lt;210&gt; 13

&lt;211&gt; 80

<212> DNA

<400> 13

cgtgagccgc atgactgcag 80

<210> 14

&lt;211&gt; 67

## <212> DNA

<400> 14

ggctcac 67

<210> 15

<211> 67

## <212> DNA

<400> 15

accacat 67

&lt;210&gt; 16

&lt;211&gt; 34

<212> DNA

<213> Artificial Sequence

<400> 16

aagatatcgc ggccgcatgg tgagcaaggg cgag

34

<210> 17

<211> 31

<212> DNA

<213> Artificial Sequence

<400> 17

aaggatccga attcttgtag agctcgtcca t

31

<210> 18

<211> 32

<212> DNA

<213> Artificial Sequence

<400> 18

atgcggccgc caccatggac tacaaagacg at

32

<210> 19

<211> 30

<212> DNA

<213> Artificial Sequence

<400> 19

cgggatcctc agtctgagtc aggcccttct

30

CGTCTTCT